

B1
C1
B2
(EF-1A)¹². In this report we refer to the transcription factor as GABP and to the motif as the N-box.

Please delete the paragraph at page 25, line 8 through page 26, line 2, and add the following paragraph at page 25, line 8:

Mouse 3T3 cells were treated for 2 h with diethyl maleate (DEM), a glutathione (GSH)-depleting agent, in the presence or absence of N-acetylcysteine (NAC), an antioxidant and a precursor of GSH synthesis. Following treatment, the cells were harvested, and nuclear extracts were prepared in the absence of a reducing agent. GABP DNA binding activity was measured by EMSA analysis using oligonucleotide probes containing a single N-box (SEQ. ID. NO. 3) or two tandem N-boxes (SEQ. ID. NO. 11). Treatment of 3T3 cells with DEM resulted in a dramatic decrease in the formation of the GABP heterodimer (GABP α GABP β , (Martin 1996⁸⁹, Fig. 2A, lane 2) and heterotetramer (GABP α_2 GABP β_2 (Ibid, Fig. 2A, lane 6) complexes on the single and double N-box. Inhibition of GABP DNA binding activity by DEM treatment was prevented by simultaneous addition of NAC (Ibid, Fig. 2A, lane 4 and 8). The reduction of GABP DNA binding activity was not due to loss of GABP protein since the amount of GABP α and GABP β 1 was unaffected by DEM or NAC treatment. Dithiothreitol (DTT) is an antioxidant. DTT treatment of nuclear extracts prepared from DEM-treated 3T3 cells restored GABP binding activity. Treatment of 3T3 nuclear extracts with 5 mM GSSG nearly abolished GABP DNA binding. Based on these observations Martin *et al.*, concluded that GABP DNA binding activity is inhibited by oxidative stress, i.e. GSH depletion. The study also measured the effect of DEM treatment on expression of transiently transfected luciferase reporter constructs containing a TATA box with either upstream double N-box or C/EBP binding site (Ibid, Fig. 4). DEM treatment had no effect on luciferase expression from C/EBP-TA-Luc after 6 or 8 h treatment (Ibid, Fig. 4). However, DEM treatment of cells transfected with double N-box-TATA-Luc, resulted in a 28% decrease in luciferase expression after 6 h and a 62% decrease after 8 h (Ibid, Fig. 4). Based on these results, Martin *et al.*, concluded that glutathione depletion inhibits GABP DNA binding activity resulting in reduced expression of GABP-regulated genes.

Please delete the paragraph at page 42, lines 16-23, and add the following paragraph at page 42, line 16:

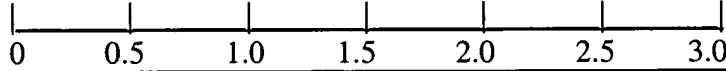
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B3 Mutation of the proximal N-box (SEQ. ID. NO. 3) to SEQ. ID. NO. 12 eliminated the DNA-protein complex formation (Pan 1998, Fig. 6C). BAEC transfected with a reporter gene directed by the murine P-selectin promoter with the mutated N-box showed a 2-10-fold increased expression compared to the wild-type promoter (Ibid, Fig. 6F). The increased transcription indicates that binding of the Ets related factor to the proximal N-box represses the P-selectin gene. Deletion of the distal N-box had no effect on the reporter gene expression. The increase transcription of the mutated gene indicates that GABP is a repressor of P-selectin.

Please delete the table at page 44, between lines 10 and 11, and add the following table on page 44, after line 10:

B4

| Gene | Sequence | Dist.* |
|--|--|-----------------|
| Murine Laminin B2 (SEQ. ID. NO. 13) | <u>CTTCCTCCTGGGCGCGCTCTCGAGTGC</u> <u>CGCGCTCGGAAG</u> | 26 bp 3.0 HT |
| Human Type IV collagenase (SEQ. ID. NO. 14) | <u>TTTCCGCTGCATCCAGACTTCCT</u> | 11 bp 1.5 HT |
| Human CD4 (SEQ. ID. NO. 15) | <u>AGGAGCCTTGCCATCGGGCTTCCT</u> | 12 bp 1.5 HT |
| Murine CD4 (SEQ. ID. NO. 16) | <u>AGGAGCCTCACGACCAGGCTTCCT</u> | 12 bp 1.5 HT |
| Murine COX Vb (SEQ. ID. NO. 17) | <u>CGGAAGTCCCGCCCATCTTGCTCAGCCTGTTCCCGGAAG</u> | 27 bp 3.0 |
| Murine COX IV (SEQ. ID. NO. 18) | <u>CTTCCGGTTGCGGGCCCCGTTCTTCCG</u> | 15 bp 2.0 HT |
| Ad2-ML (SEQ. ID. NO. 19) | <u>CGTCCTCACTCTCTTCCG</u> | 6 bp 1.0 HT |
| Helical turns |  | |

Please add the following sequence listing on page 172 between the end of the specification on page 171 and the claims.

SEQUENCE LISTING

B5 <110> Polansky, Hanan

<120> MICROCOMPETITION AND HUMAN DISEASE



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<140> 09/732,360
<141> 2000-12-07
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<170> PatentIn version 3.1
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<301> Yu M et al.

<302> GA-binding protein-dependent transcription initiator elements. Effect of helical spacing between polyomavirus enhancer A factor (PEA3)/Ets-binding sites on initiator activity

<303> Journal of Biological Chemistry

<304> 272

<305> 46

<306> 29060-7

<307> 1997-11-14

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<303> Journal of Biological Chemistry

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<302> GA-binding protein-dependent transcription initiator elements. Effect of helical spacing between polyomavirus enhancer A factor (PEA3)/Ets-binding sites on initiator activity

<303> Journal of Biological Chemistry

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<302> GA-binding protein-dependent transcription initiator elements. Effect of helical spacing between polyomavirus enhancer A factor (PEA3)/Ets-binding sites on initiator activity

<303> Journal of Biological Chemistry

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18

REMARKS

The communication of February 11, 2002 has been reviewed and its contents carefully noted. Reconsideration of this case, as amended, is requested. Claims 1 through 50 remain in this case.

The specification has been amended to include a sequence listing, as well as references to the sequence identification numbers in the sequence listing. A paper copy and a copy of the sequence listing in computer readable form are also attached. No new matter has been added.